

February 15, 1950.

Mr. Ellis Englesberg,
Dept/ Bacteriology,
University of California,
Berkeley 4, Calif.

Dear Englesberg:

Enclosed are your application forms with Dr. Brink's endorsement as requested.

In general, your prospectus seems satisfactory. However, I think that it might be worthwhile having it retyped more neatly by a professional typist, as it is long enough to be somewhat tiring to read in its present form. If you have time to revise, I would recommend that somewhat more emphasis be put on the general problem, viz., the conditions of spontaneous mutation, and the possible role of normal metabolites. To the list of substances with such functions, which should be investigated, might be added peroxides and (in mammals, at any rate) cyanate [from urea]. After the generalized statement would be the more appropriate point to mention the more specific lines of approach — the correlation with growth, and the particular work with formaldehyde. I think that it might be advisable to stress that your predoctoral experience has been primarily biochemical and bacteriological, and that the postdoctorate fellowship might serve to widen your experience with genetic techniques and concepts. That is, a postdoctoral fellowship should have a broader function than the prolongation of a predoctoral research project. I think that it would not be inappropriate to insinuate this under section 9. The final paragraph of this section as it stands is somewhat sophomoric, and the thought is probably best put as the introductory statement of the problem.

To turn to a more scientific issue, I have lately been studying the mechanism of bactericidal action of a number of compounds, including formaldehyde, on diploid strains of *E. coli* K-12. Formaldehyde seems to kill in much the same way as UV and nitrogen mustard, by chromosomal or nuclear inactivation [I leave to your imagination how this can be shown with the help of heterozygous diploid stocks], and I am therefore a little surprised at your conclusion that it is not mutagenic for *coli* B. Did you allow for phenotypic lag in looking for induced phage-resistance mutants? I would be interested to hear any details of your experiments that you can conveniently transmit.

Yours with best wishes,

Joshua Lederberg